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(54) Title of Invention

Laboratory in a disk

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En 27.02.1998

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AT21
G1B BCB

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EP0707076 A1
EP0417305 A1
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(continued on next page)

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WO93/20092 A1
Carol T Schembri et al, "Portable simultaneous multiple analyte whole blood for point-of-care testing", Clinical Chemistry vol. 38, no. 9, September 1992, pages 1665-1670.

(58) Field of search

As for published application 2337113 A *viz:*
INT CL[6] C12Q, G01N
updated as appropriate

FIG. 1

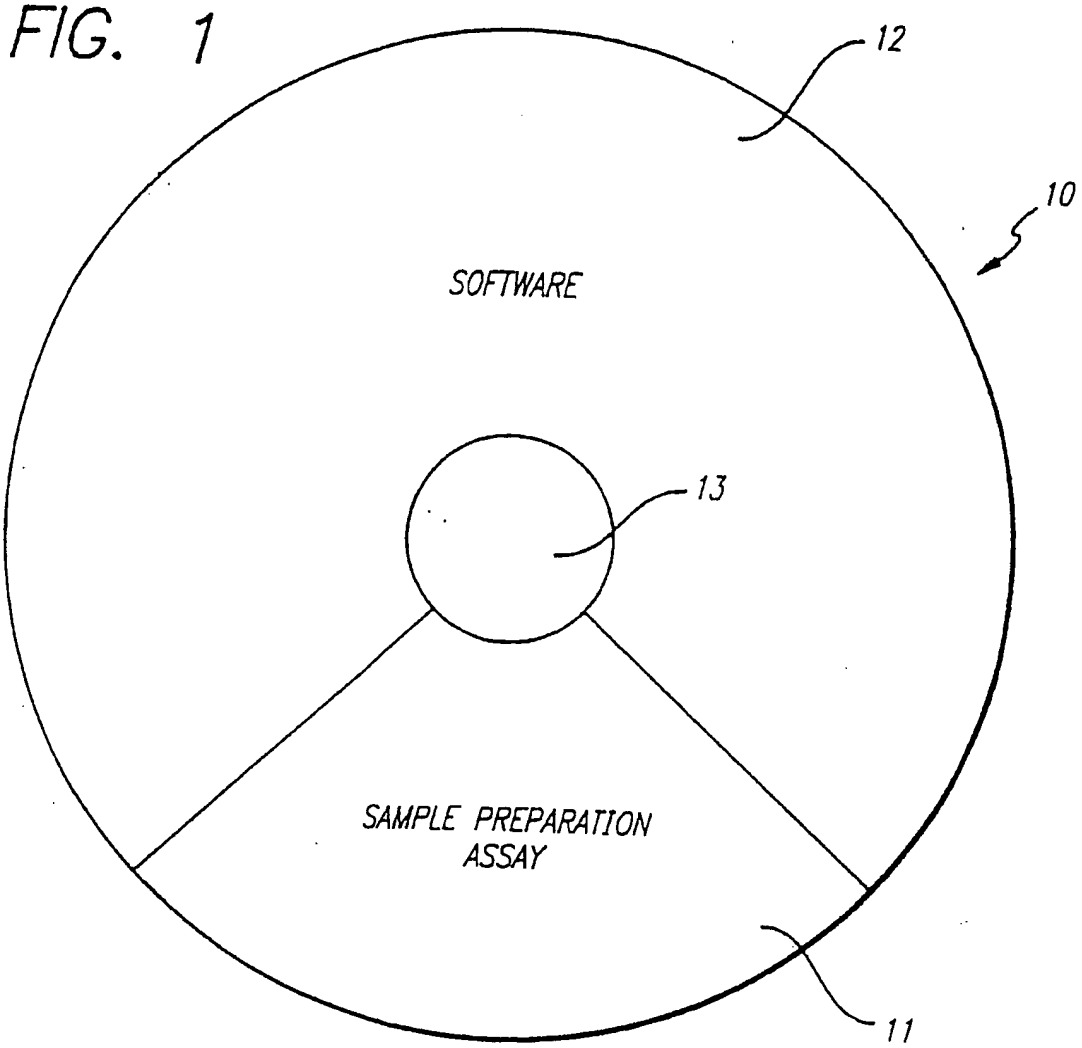

12
10
SOFTWARE
13
SAMPLE PREPARATION
ASSAY
11

FIG. 2A

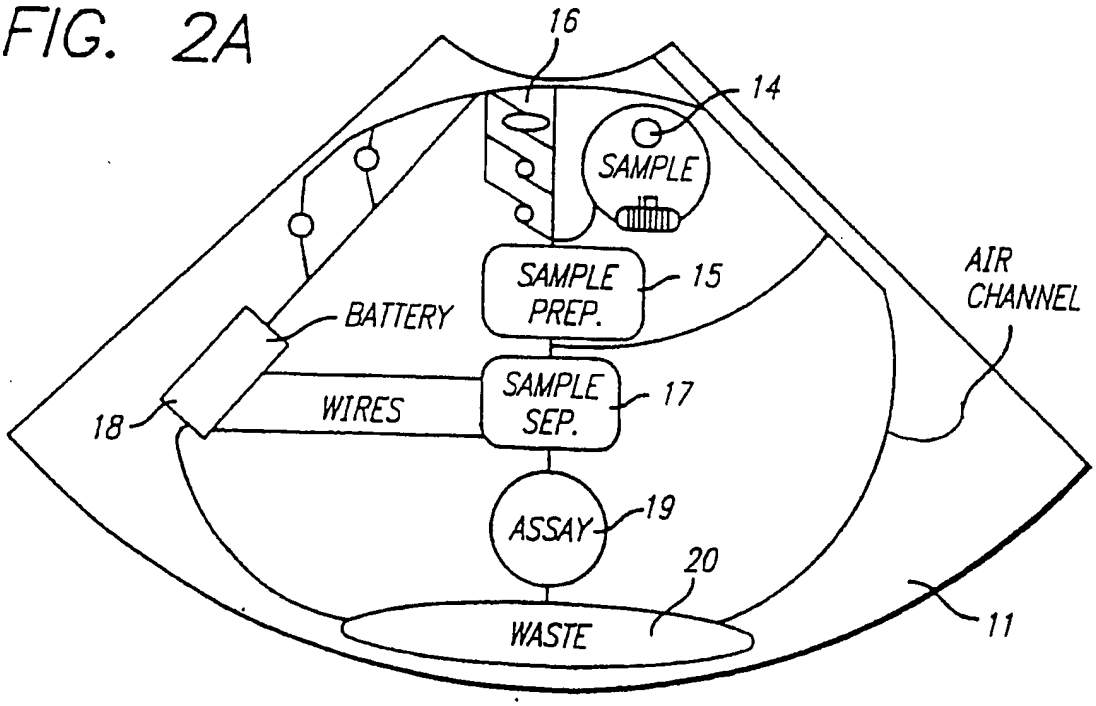

16
14
SAMPLE
SAMPLE
PREP.
15
AIR
CHANNEL
BATTERY
WIRES
SAMPLE
SEP.
17
18
ASSAY
19
20
WASTE
11

FIG. 2B

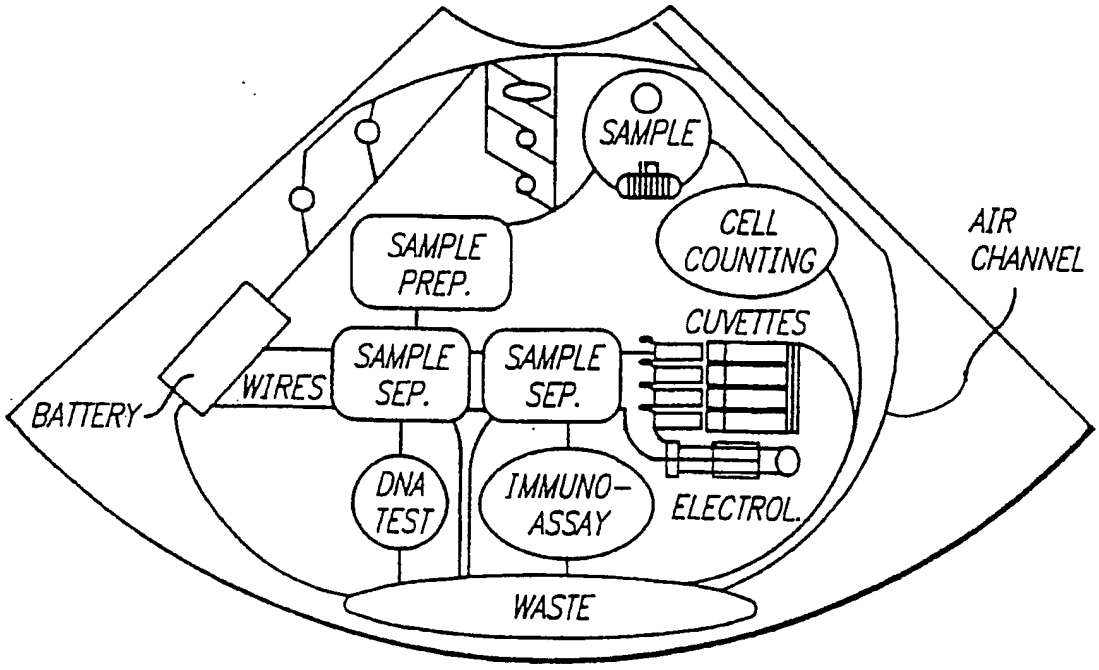

SAMPLE
CELL COUNTING
AIR CHANNEL
SAMPLE PREP.
CUVETTES
SAMPLE SEP.
SAMPLE SEP.
WIRES
BATTERY
DNA TEST
IMMUNO-ASSAY
ELECTROL.
WASTE

FIG. 3

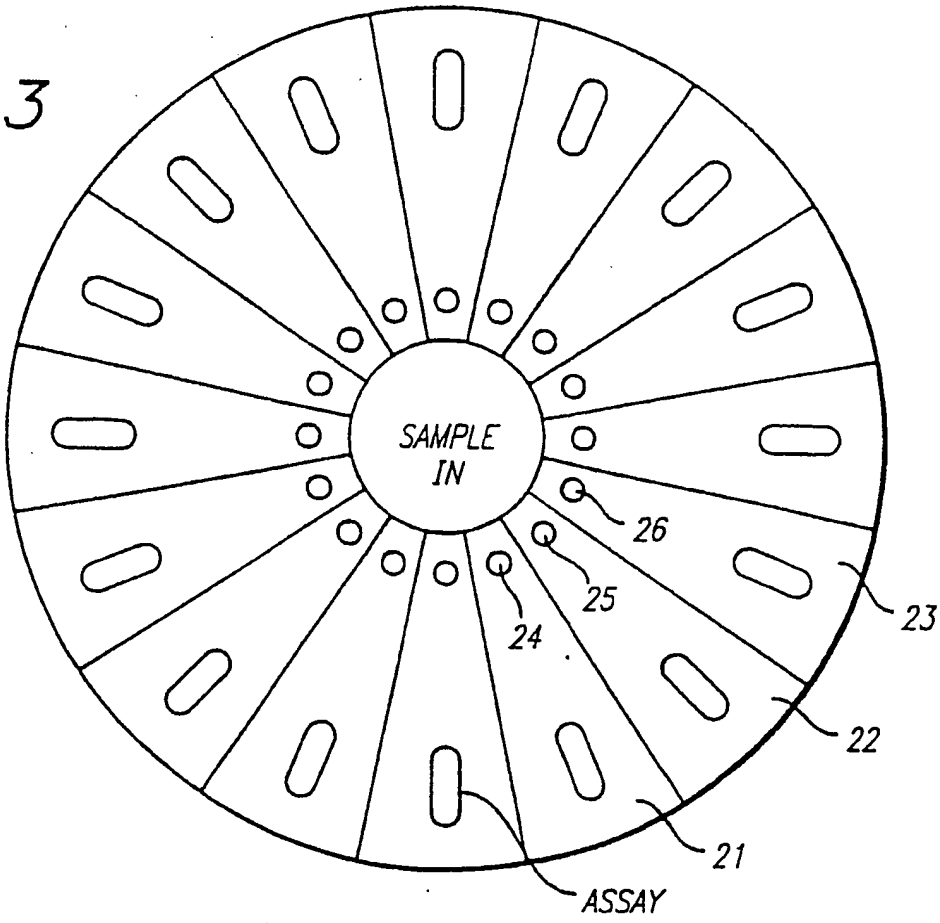

SAMPLE IN
26
25
24
23
22
21
ASSAY

FIG. 4

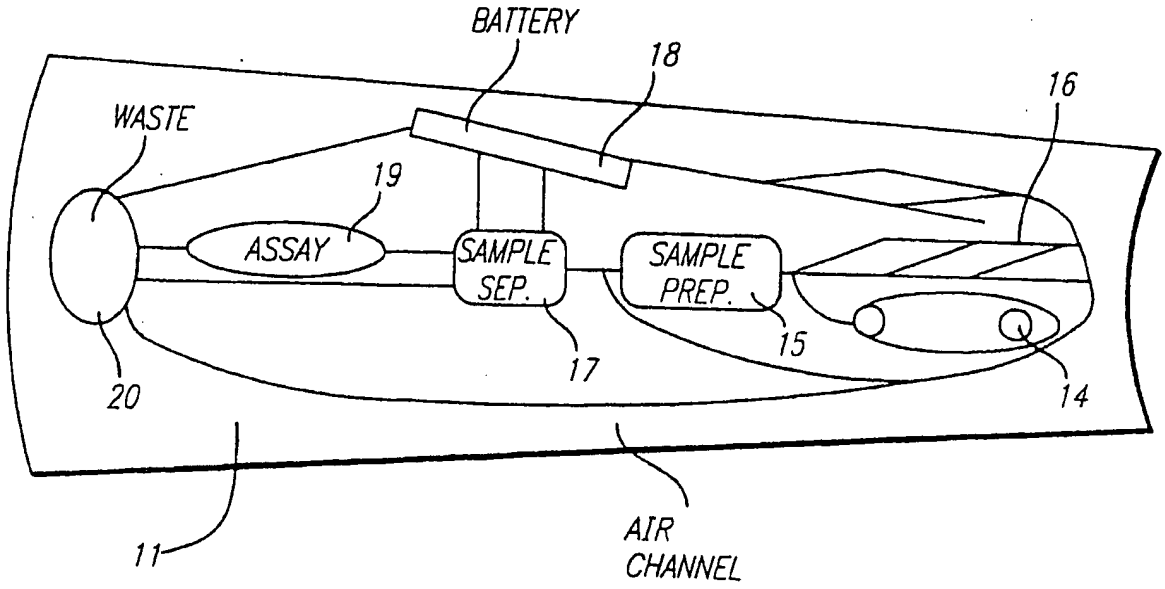

BATTERY
18
16
WASTE
19
ASSAY
SAMPLE SEP.
SAMPLE PREP.
15
17
20
14
11
AIR CHANNEL

FIG. 5

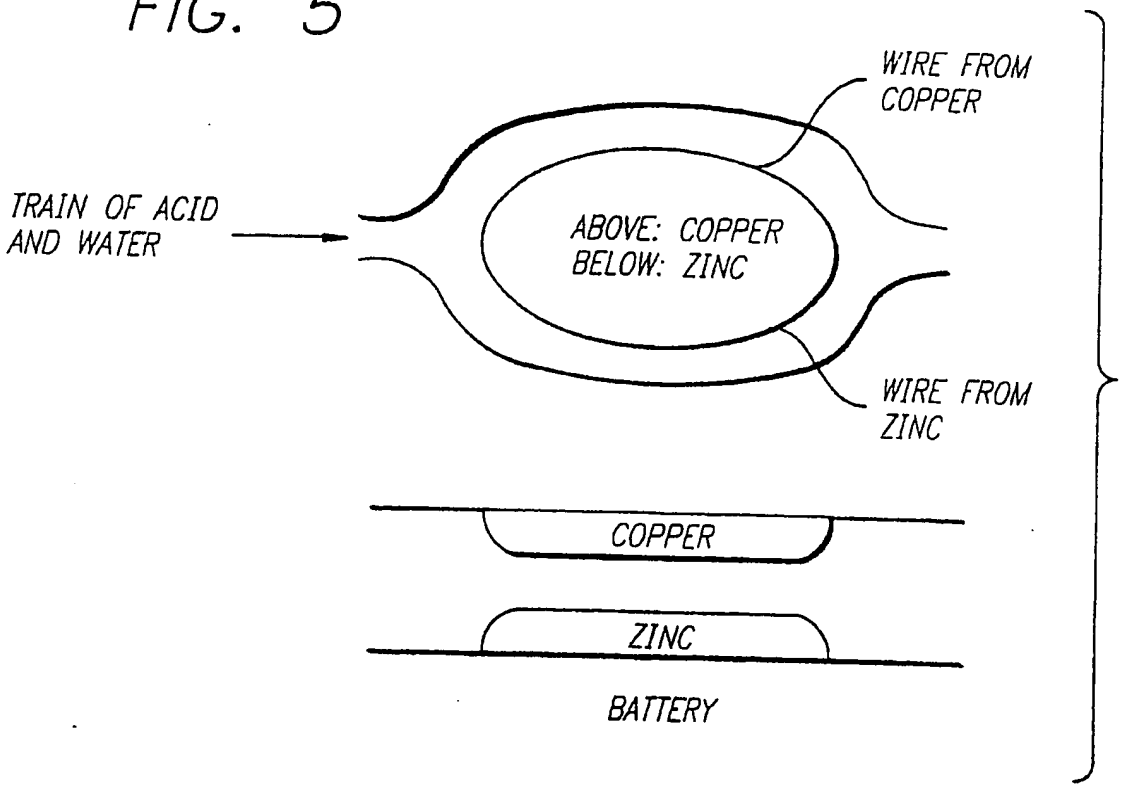

WIRE FROM COPPER
TRAIN OF ACID AND WATER
ABOVE: COPPER
BELOW: ZINC
WIRE FROM ZINC
COPPER
ZINC
BATTERY

FIG. 6

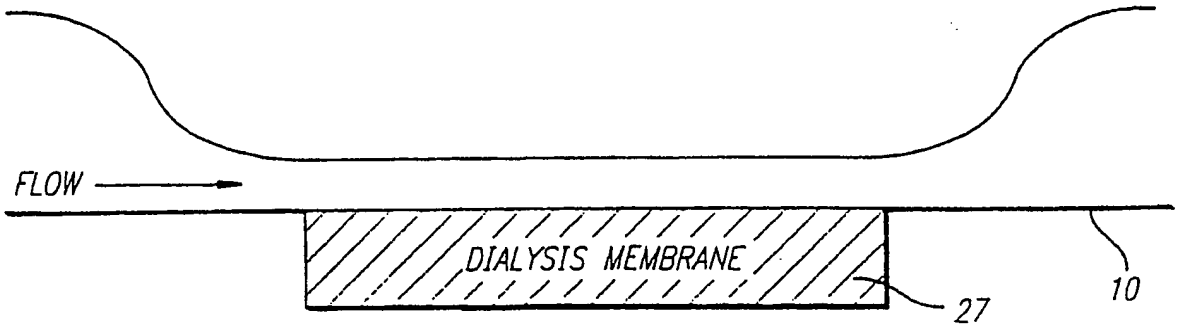

FLOW
DIALYSIS MEMBRANE
27
10

FIG. 7

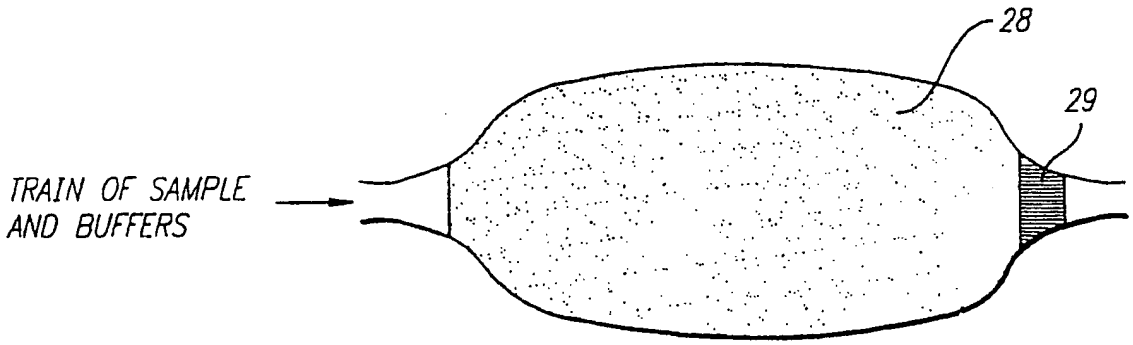
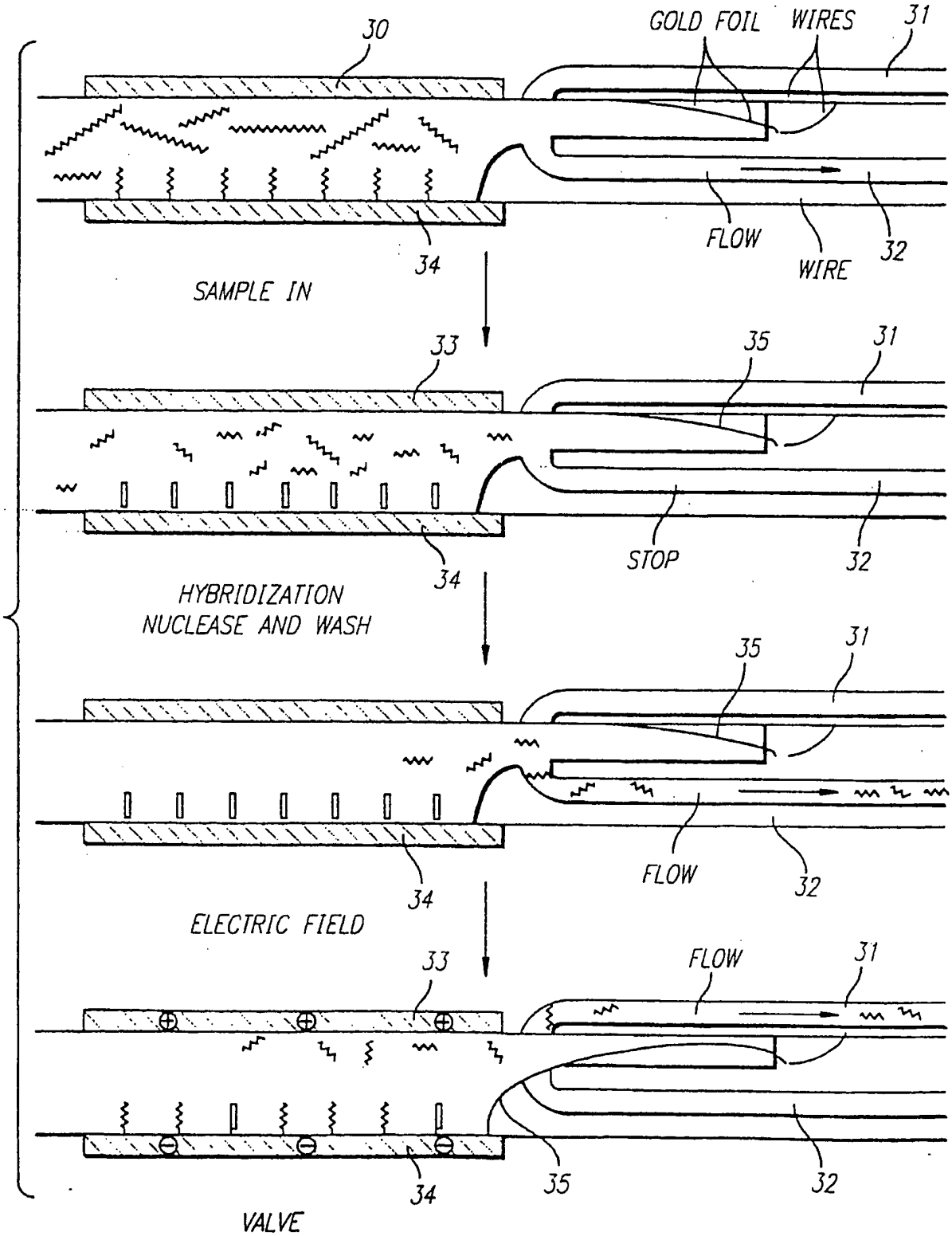

28
29
TRAIN OF SAMPLE
AND BUFFERS

FIG. 8


30
GOLD FOIL
WIRES
31
FLOW
WIRE
32
34
SAMPLE IN
33
35
31
STOP
32
34
HYBRIDIZATION
NUCLEASE AND WASH
35
31
FLOW
32
34
ELECTRIC FIELD
33
FLOW
31
34
35
32
VALVE

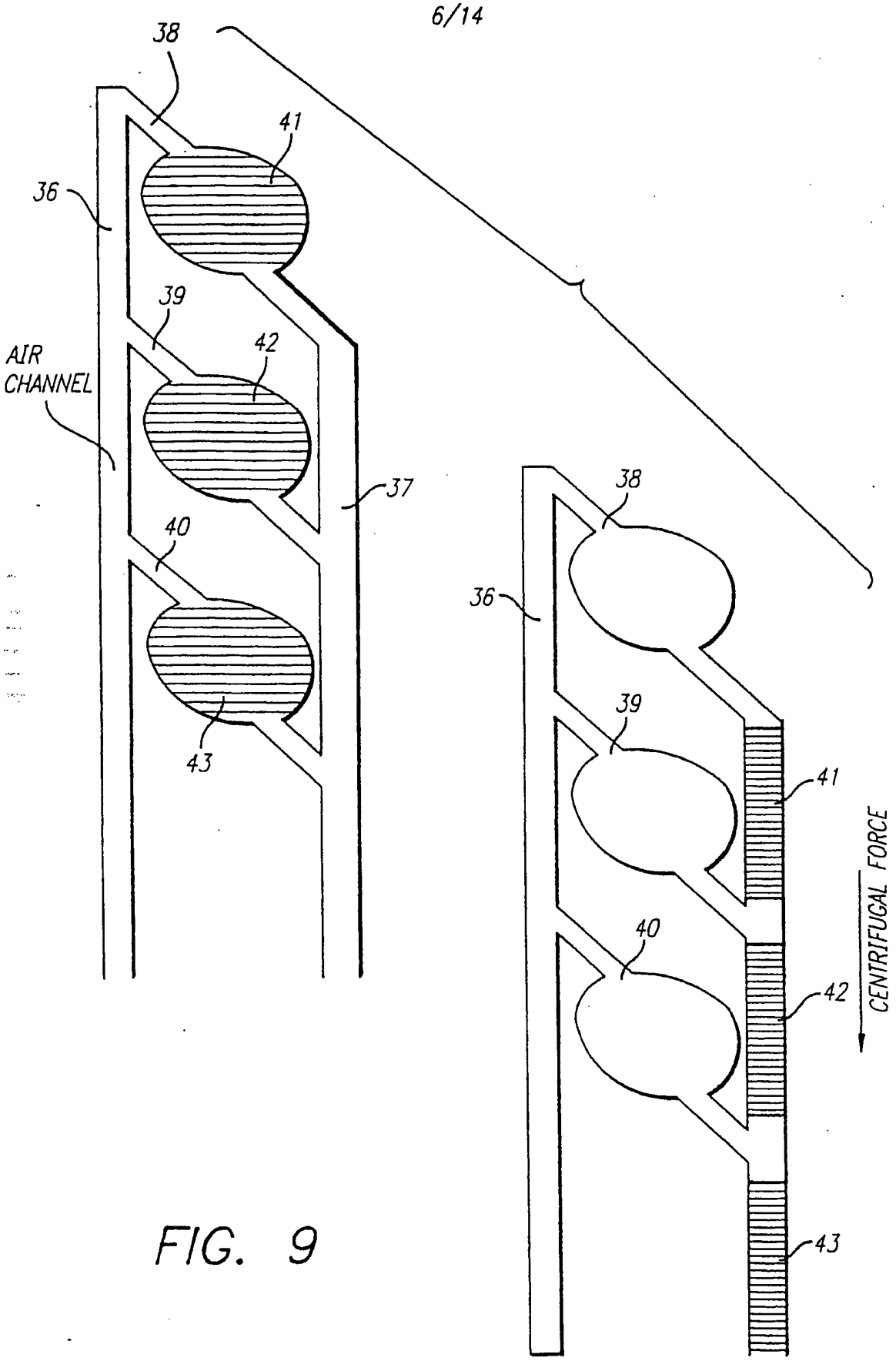

38
41
36
39
AIR
CHANNEL
42
37
40
43
38
36
39
41
CENTRIFUGAL FORCE
40
42
43

FIG. 9

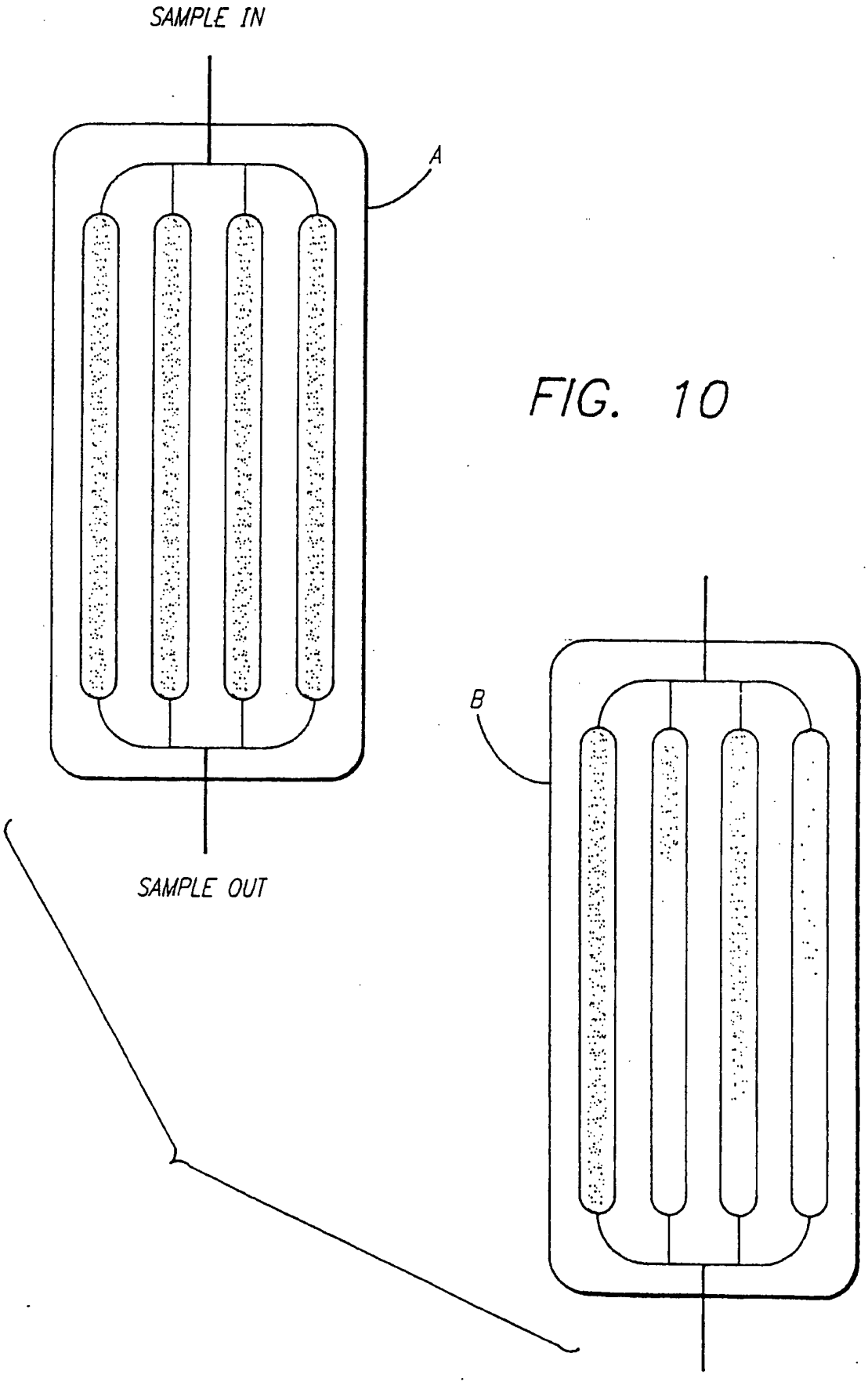


FIG. 10

FIG. 11A

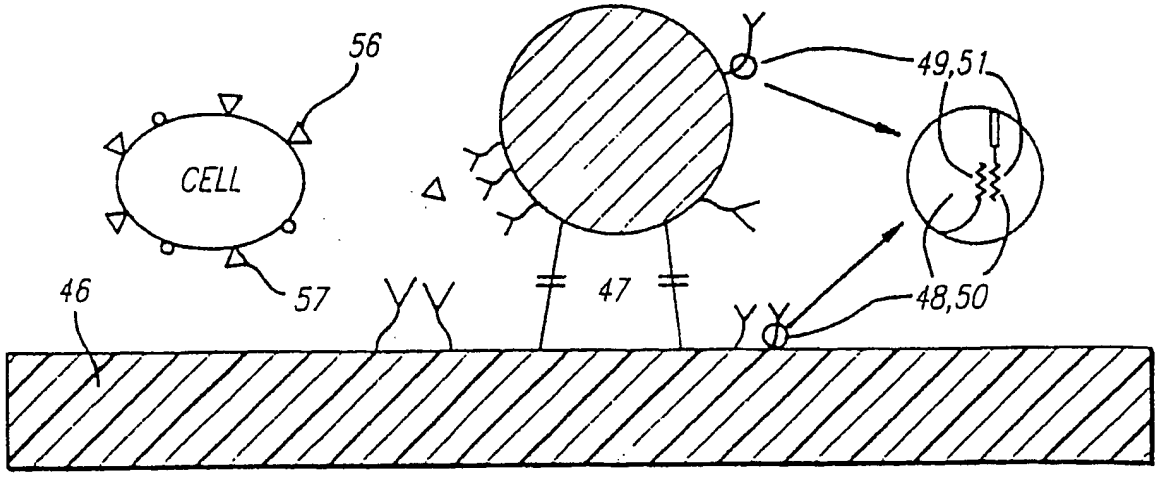


FIG. 11B

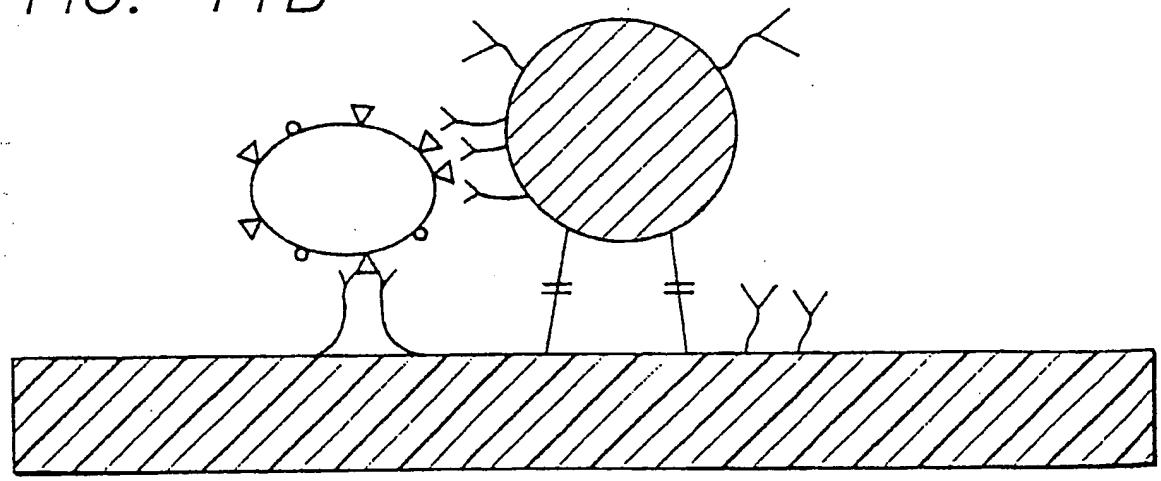


FIG. 11C

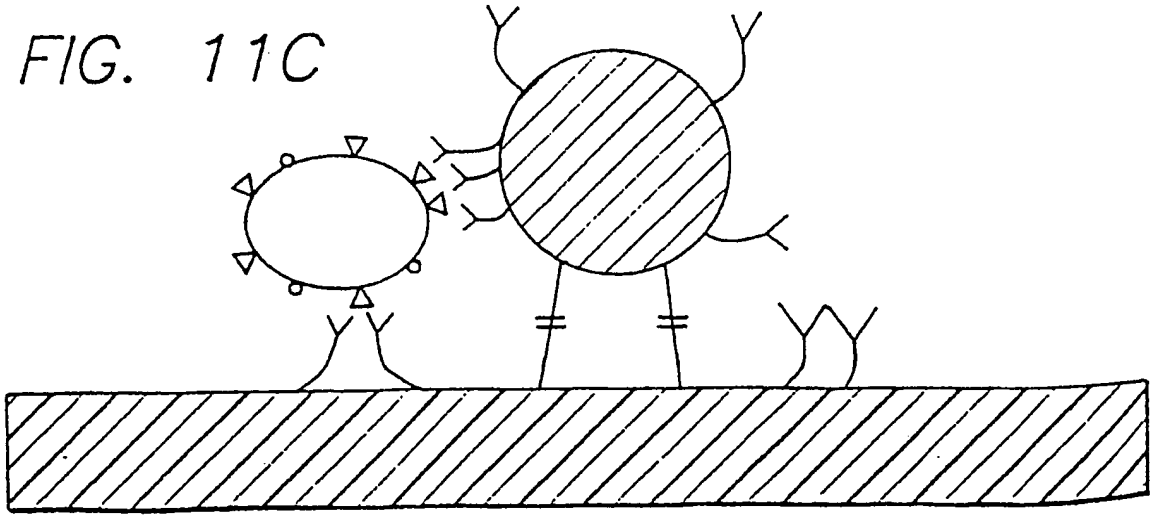


FIG. 12A

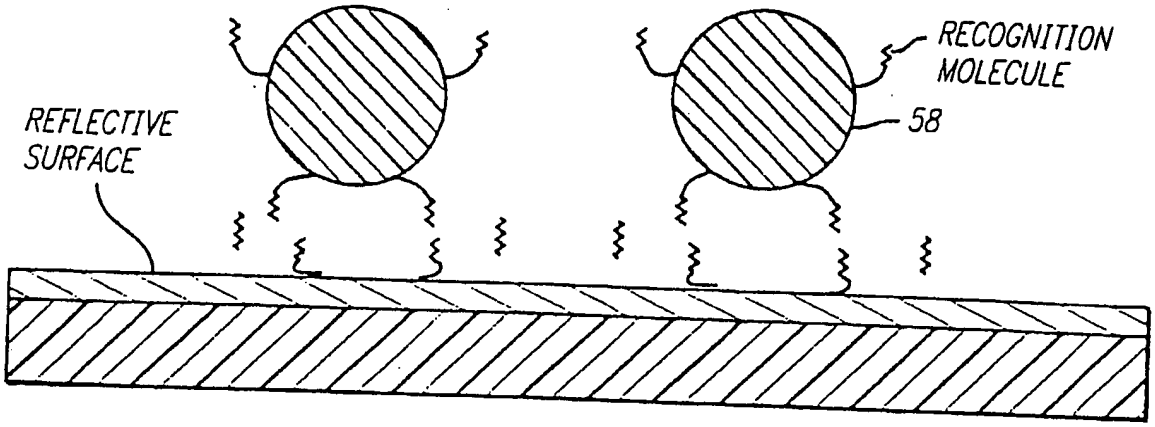


FIG. 12B

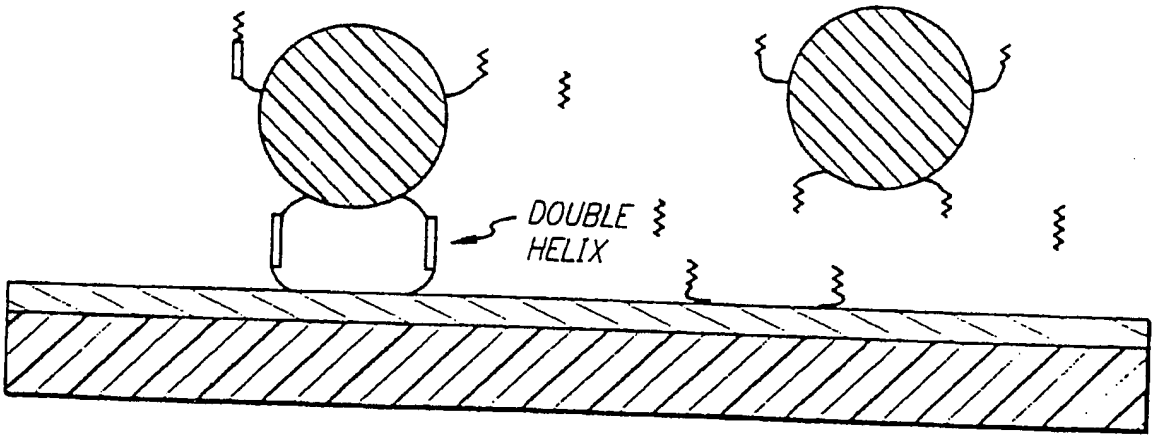


FIG. 12C

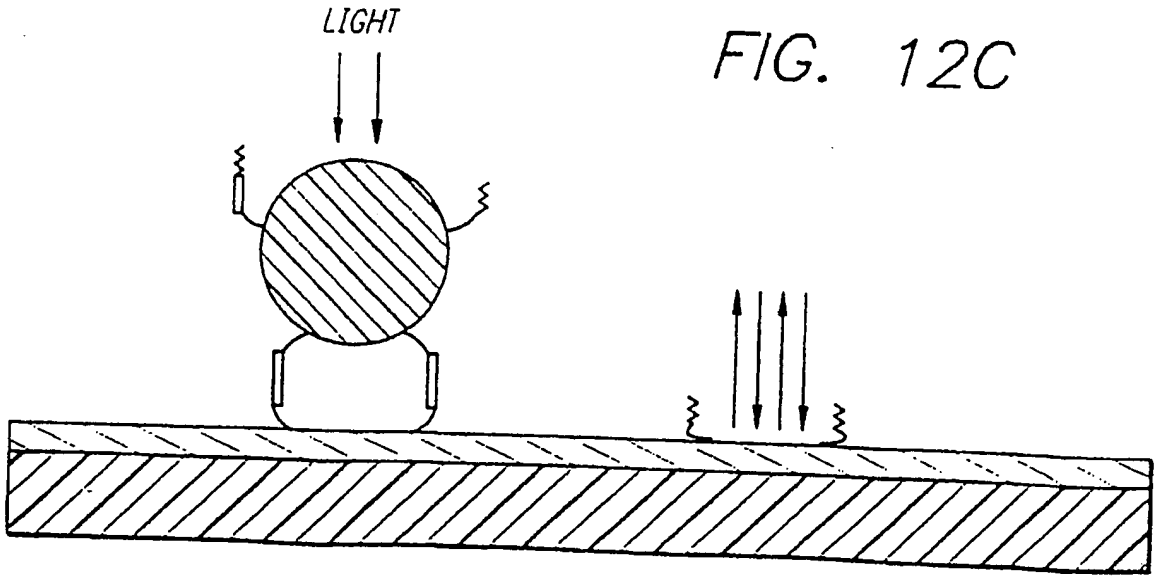


FIG. 13

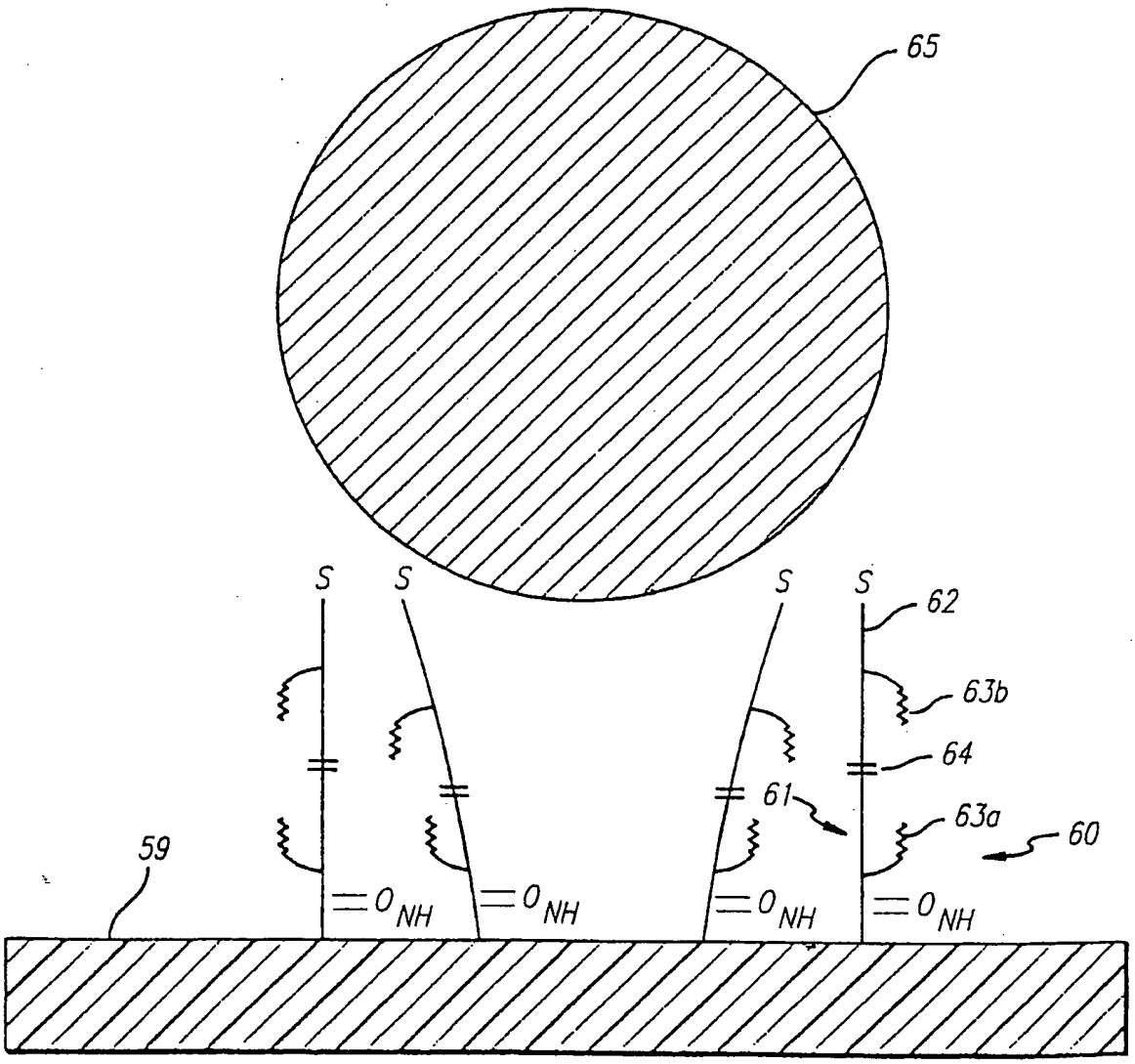


FIG. 14a

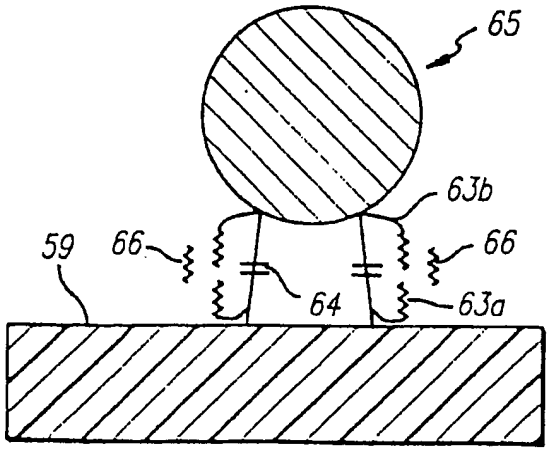


FIG. 14b

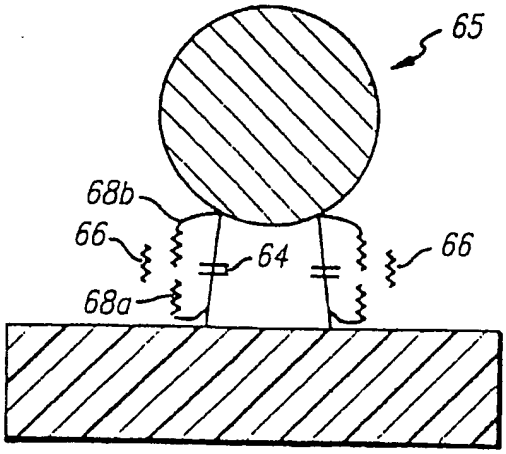


FIG. 14c

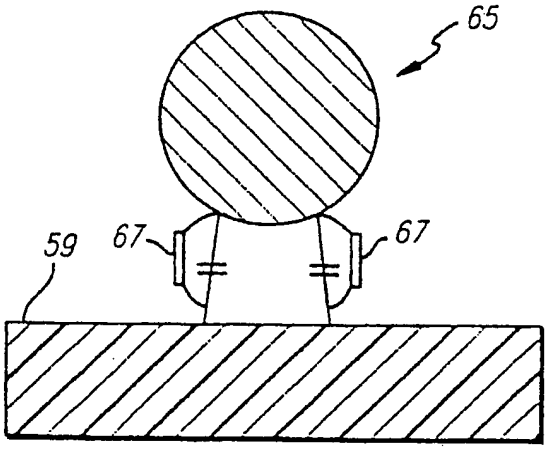


FIG. 14d

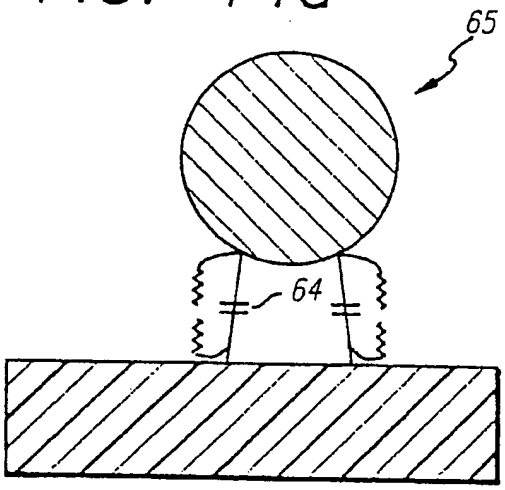


FIG. 14e

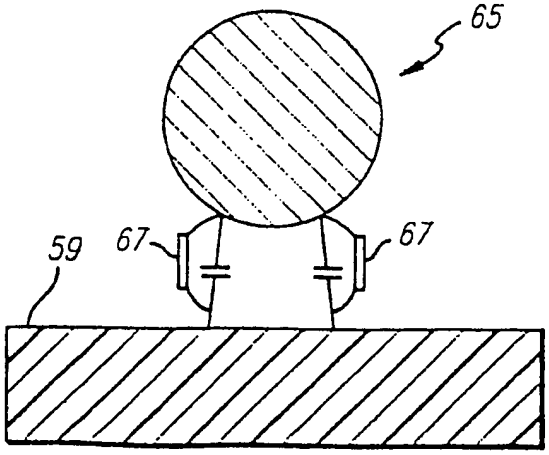


FIG. 14e

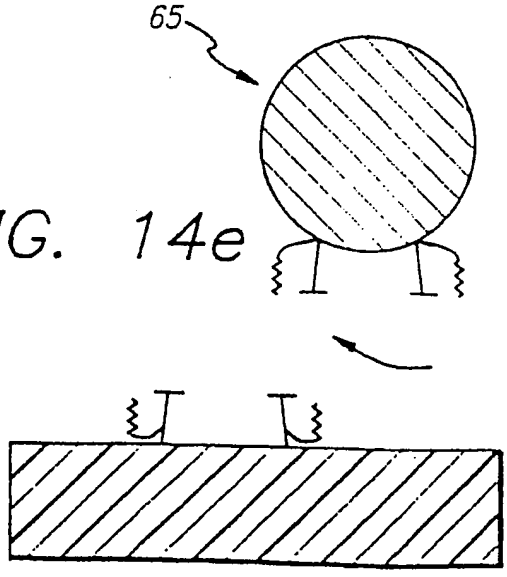


FIG. 15A

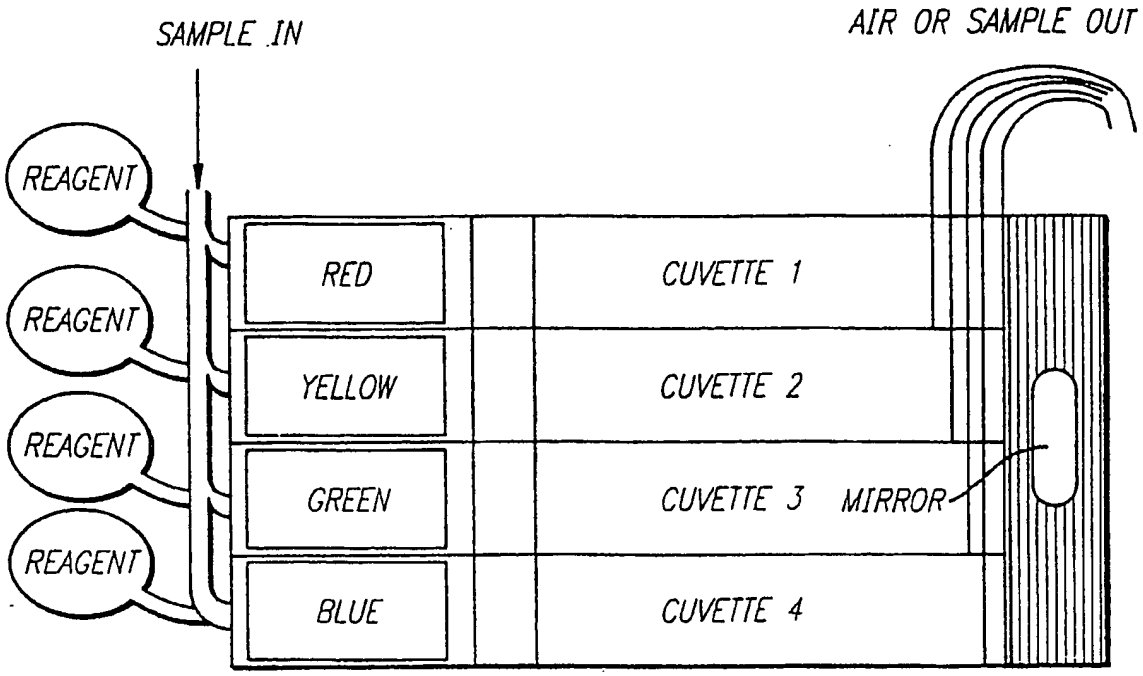
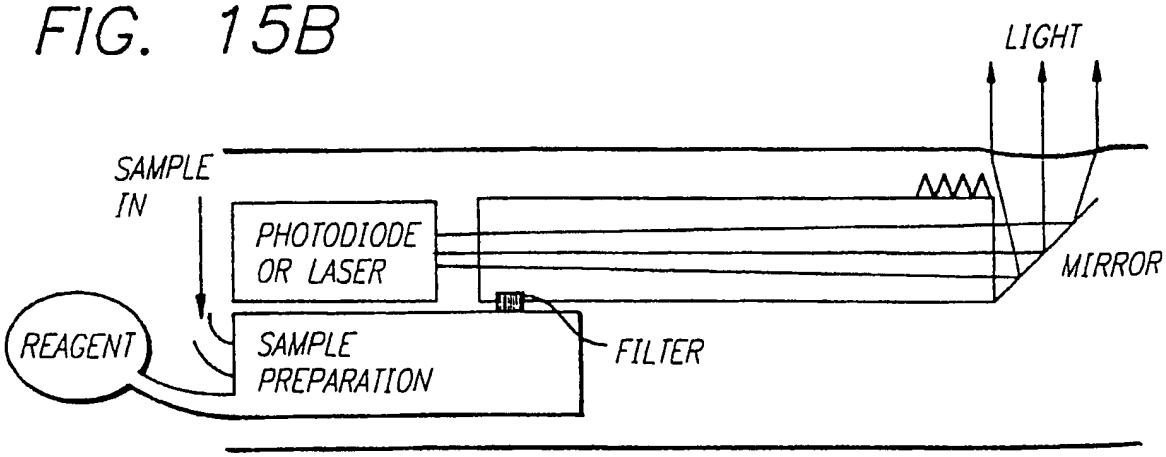
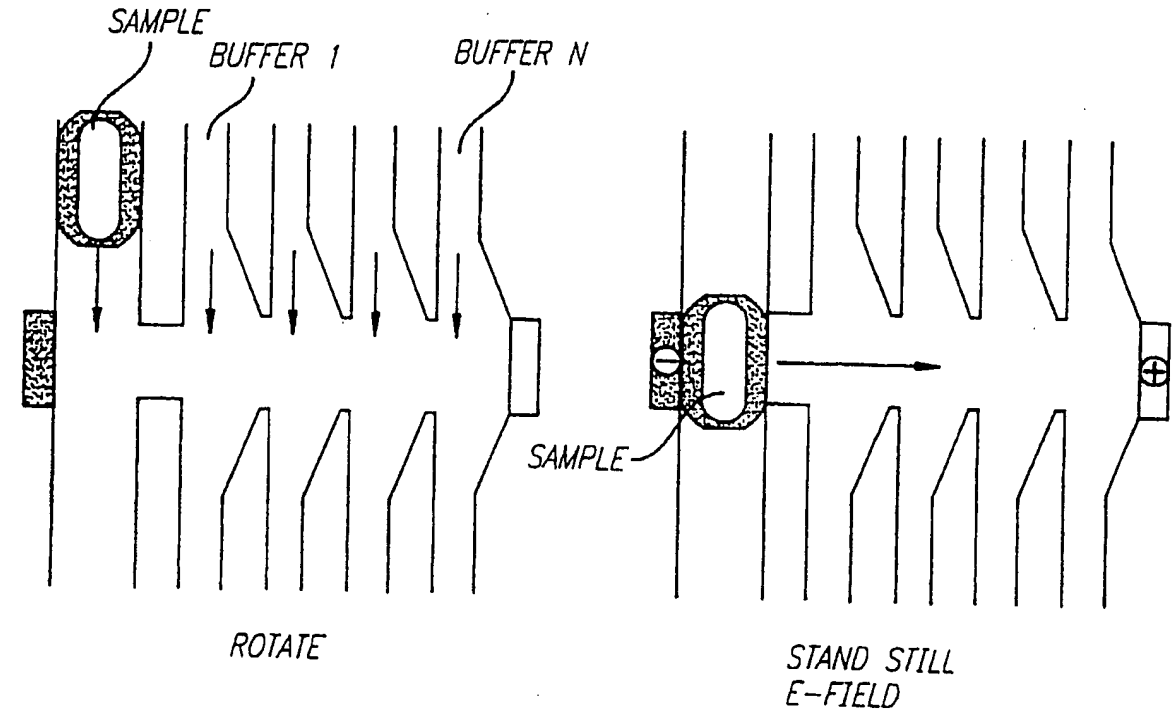


FIG. 15B



CUVETTE ASSEMBLY

FIG. 16


SAMPLE
BUFFER 1
BUFFER N
SAMPLE
ROTATE
STAND STILL
E-FIELD

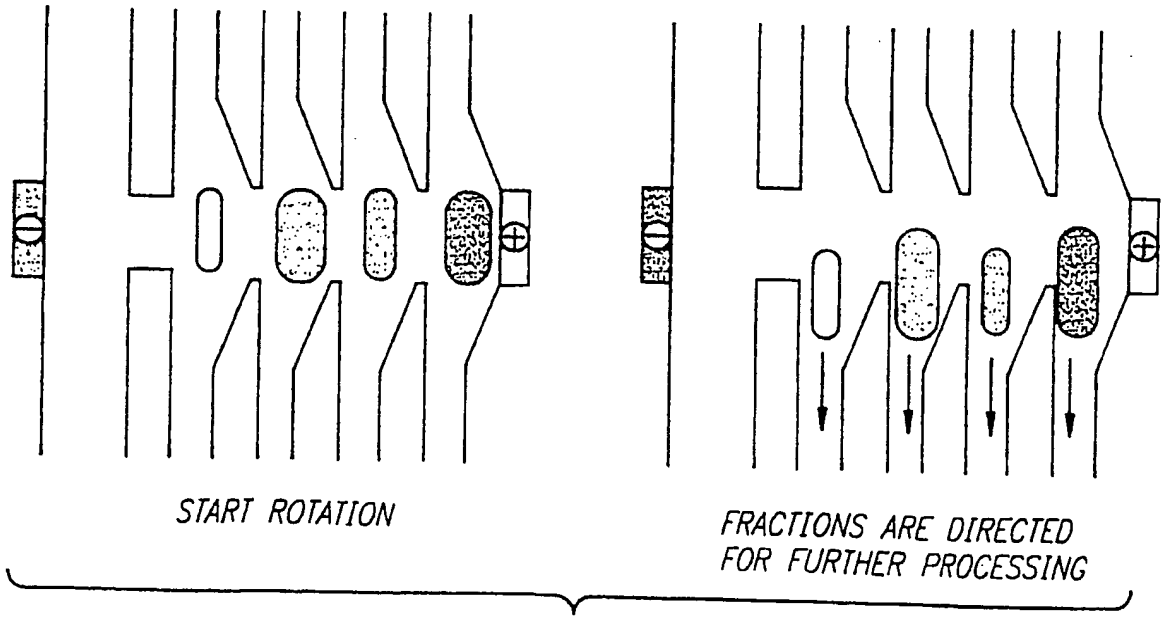
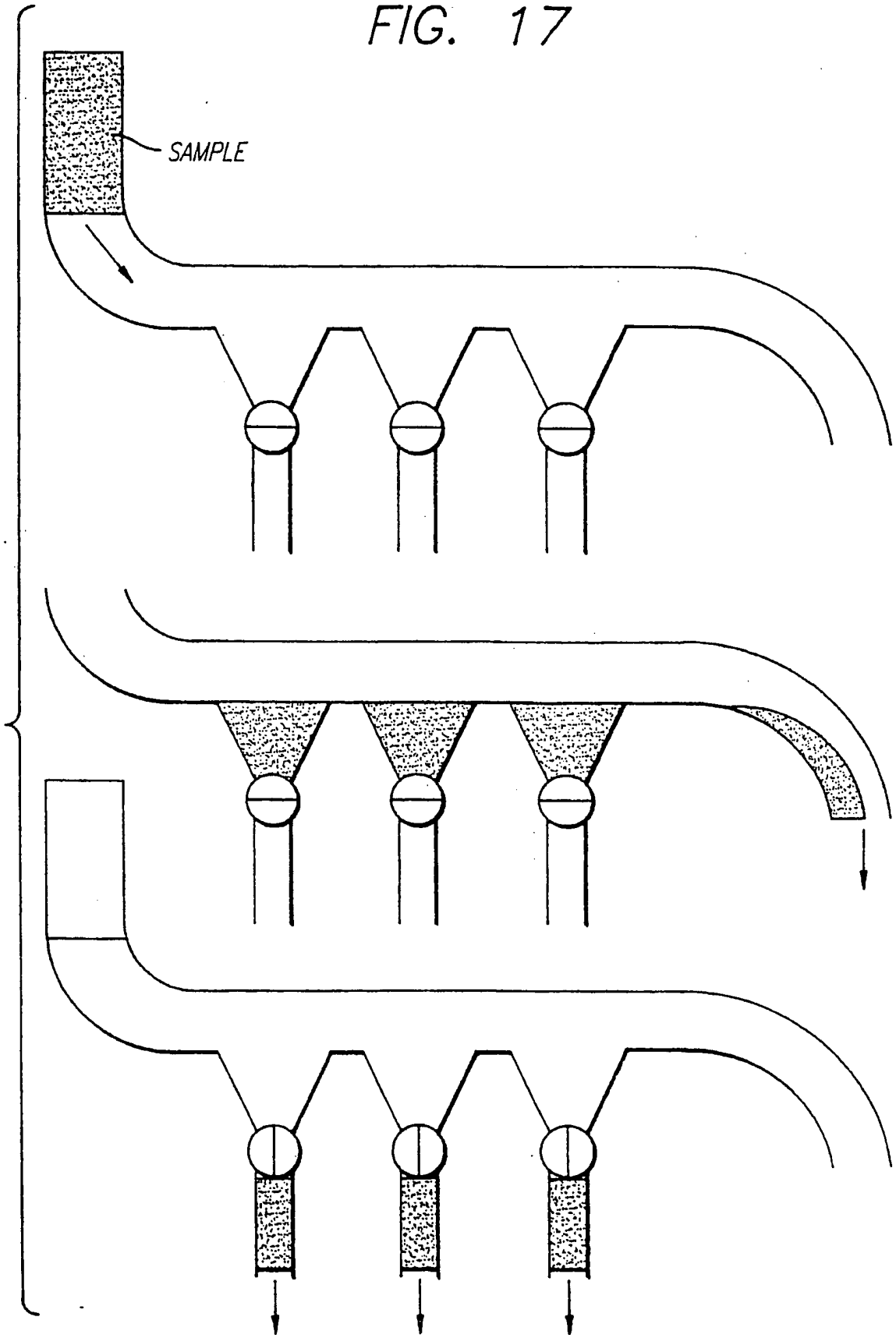

START ROTATION
FRACTIONS ARE DIRECTED
FOR FURTHER PROCESSING

FIG. 17



LABORATORY IN A DISK

FIELD OF THE INVENTION

This invention relates generally to diagnostic assays and methodology therefor. In particular, it relates to diagnostic assay components configured on a compact optical disk and methodology for the use thereof.

BACKGROUND

There is an enormous need to make clinical assays faster, cheaper and simpler to perform. Ideally patients should be able to test themselves, if so desired. One way towards this goal has been through miniaturization and integration of various assay operations. Currently, a number of bio-chip assays (so-called because some are built using silicon chip photolithography techniques) are commercially available or under development. All of these approaches require a reading machine and a computer.

Disk-shaped cassettes used for clinical assays in conjunction with UV/Vis spectrometry are also commercially available. U.S. Patent No. 5,122,284 describes a centrifugal rotor that contains a number of interconnected fluid chambers connected to a plurality of cuvettes. The rotor is adapted to be utilized with a conventional laboratory centrifuge, and is formed of materials that allow photometric detection of the results of assays that have been carried out in the reaction cuvettes. A large number of rotor configurations and related apparatus for the same or similar types of analysis have been described. See for example U.S. Patents 5,472,603; 5,173,193; 5,061,381; 5,304,348; 5, 518,930; 5,457,053; 5,409,665; 5,160,702; 5,173,262; 5,409,665; 5,591,643; 5,186,844; 5,122,284; 5,242,606; and patents listed therein. Lyophilized reagents for use in such systems are described in U.S. Patent 5,413,732.

The principles of a centrifugal analyzer have been adapted into a disk that can be used in a CD-drive like instrument (Mian, et al., WO 97/21090 Application). Mian

teaches a modified CD-drive with a dual function: 1. It is used to read information stored in the disk, and 2. It is used to rotate the disk. However, Mian does not teach utilization of the reading capability of a CD-drive for actual assay analysis.

Notwithstanding recent advances, there remains a need for a simpler assay configuration that performs assays quickly, efficiently, accurately and at low cost. The present invention combines diagnostic assays with computers and compact disk technology. In its most preferred embodiment, a computer with a compact disk reader is the only instrument needed. All chemistry is performed inside a compact disk that may be referred to as an integrated biocompact disk (IBCD). The same compact disk is also encoded with software, i.e., machine-readable instructional and control information, that provides instructions to a computer prior to, during and after the assay.

CDs or DVDs represent the most economical and in many ways best information storage media. It must be noted that CD and DVD are currently used acronyms that may change in the future even if the underlying technology stays basically the same. A CD- or DVD-drive is in several respects equivalent to a scanning confocal microscope. At the same time these instruments are comparable to good centrifuges, because in commercial drives the rotation frequency is between 200-12,000 rpm and can be adjusted within certain limits. Combining these three features into the same analytical system results into great simplification as compared with any other analytical technique. Yet, the performance is comparable or better than in most competing methods. Although this invention requires slightly modified CD- or DVD-drives, it is possible to incorporate these changes into commercial drives. This will enable Point-Of-Patient-Care (POPC) and home use of this invention. Use of CD- or DVD-drives will allow accurate digital analysis of any sample without any specific analytical instrumentation.

SUMMARY OF THE INVENTION

In one aspect, the invention is directed to an optical disk, adapted to be read by an optical reader, comprising a first sector having a substantially self-contained assay means for binding an analyte suspected of being in a sample to at least one predetermined location in the first sector and a second section containing control means for conducting the assay and analyte location information, with respect to one or more analytes suspected of being in the sample, accessible to the reader, wherein the presence or absence of the analyte at said location is determinable by the reader using the control means and the location information. Depending on the nature of the assay, the disk may include fluid storage means, fluid transfer means, such as one or more capillary ducts, valves, batteries, dialyzers, columns, filters, sources of electric fields, wires or other electrical conductive means such as metallic surface deposits and the like.

The disk may have one or more sample entry ports to deliver sample fluid to the assay sector. Such ports if present are preferably sealable so that after application of the sample to the disk, the sealed disk including the sample comprises a hermetically sealed device that may be conveniently disposed of by conventional means or other disposal mechanisms for dealing with biological waste. Also, the assay sector of the disk is conveniently divided into various subsections for sample preparation and analyte separation. A waste receptacle subsection may be conveniently provided as well. The assay sector may be divided into a multiplicity of subsectors that each receives a sample. Each such subsector may analyze for one or more analytes depending on the particular application at hand.

In another aspect the invention is directed to an apparatus for conducting an assay comprising an optical disk, a disk reader and an information processor, the disk comprising a first sector having substantially self-contained assay means for localizing an analyte suspected of being in a sample to at least one, predetermined location in the

first sector and a second sector containing control information for conducting the assay and analyte location information, with respect to one or more analytes suspected of being in the sample, accessible to the reader and processable by the information processor, wherein the disk is adapted to be read by the reader and the information processor is adapted to determine the presence or absence of the analyte at said location using the control information and the location information. The apparatus may include a reader having a CD-ROM or DVD reader and an information processor, such as a personal computer.

In still another aspect the invention is directed to an optical disk, adapted to be read by a CD-ROM or DVD reader, comprising a substantially self-contained assay means in the disk for localizing an analyte suspected of being in a sample to at least one, predetermined location on the disk and means at said location for detection of the absence or presence of the analyte by the CD-ROM or DVD reader.

BRIEF DESCRIPTON OF THE DRAWINGS

Figure 1 is a schematic representation of a disk of this invention.

Figure 2 A is a more detailed schematic representation of a sample preparation and assay sector of the disk, illustrating the overall layout of a typical assay sector.

Figure 2 B is a schematic representation of an ubiquitous assay sector that is capable of performing immunoassays, DNA testing, cell counting, spectrophotometric assays and electrolyte analysis.

Figure 3 is a schematic representation of a disk of this invention illustrating a multiplicity of assay sectors, each having an individual sample inlet port.

Figure 4 is a more detailed schematic representation of one of the assay sectors illustrated in Fig. 3.